CLAIMS

What is claimed is:

1. A method of synthesizing a polynucleotide, comprising:

(a) coupling a second nucleoside to a first nucleoside through a phosphite linkage, wherein the second nucleoside has a non-carbonate protecting group protecting a hydroxyl; and

(b) exposing the product of step (a) to a composition which concurrently oxidizes the phosphite formed in step (a) to a phosphate and deprotects the protected hydroxyl of the second nucleoside.

2. A method according to claim 1 wherein the second nucleoside is a phosphoramidite and wherein steps (a) and (b) are repeated and the hydroxyl deprotected in a first iteration of step (b) reacts to form the phosphite linkage with the second nucleoside in the next iteration of step (a).

3. A method according to claim 1 wherein the non-carbonate protecting group is an acid labile protecting group and the composition comprises an acid to remove the non-carbonate protecting group.

4. A method according to claim 1 wherein the composition comprises a solution with a solvent which is primarily non-aqueous.

5. A method according to claim 4 wherein the solution is anhydrous.

6. A method according to claim 2 wherein the solution comprises iodine, an oxaziridine or a peroxide as an oxidizing agent.

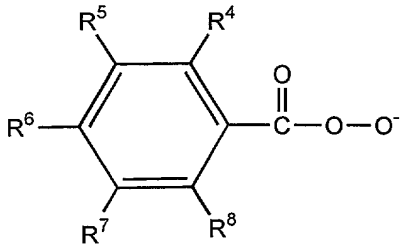
7. A method according to claim 2 wherein the composition comprises an acetic acid and iodine, an oxaziridine, or an organic peroxide.

8. A method according to claim 1 wherein the non-carbonate protecting group is labile under nucleophilic attack under neutral or mildly basic conditions and the

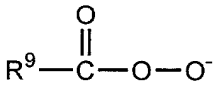
composition comprises a nucleophile that exhibits an alpha effect at neutral to mildly basic pH.

9. The method of claim 8 wherein the nucleophile is an inorganic peroxide of the formula M+OOH-, wherein M+ is a counterion selected from the group consisting of H+, Li+, Na+, K+, Rb+ and Cs+.

10. The method of claim 8, wherein the nucleophile is an organic peroxide of the formula (V), (VI) or (VII),



(V)



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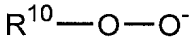


(VII)

in which R4 through R10 are hydrocarbyl optionally substituted with one or more nonhydrocarbyl substituents and optionally containing one or more nonhydrocarbyl linkages.

11. The method of claim 8 wherein the nucleophile is one of t-butyl hydroperoxide or m-chloroperoxybenzoic acid, or mixtures thereof.

12. A method of fabricating an addressable array of polynucleotides on a substrate carrying substrate bound moieties each with a hydroxyl group, comprising, at each of multiple different substrate addresses:

(a) coupling a nucleoside to a second nucleoside through a phosphite linkage, wherein the coupled nucleoside has a non-carbonate protecting group protecting a hydroxyl; and

(b) exposing the product of step (a) to a composition which both oxidizes the phosphite formed in step (a) to a phosphate and deprotects the protected hydroxyl of the coupled nucleoside;

(c) repeating steps (a) and (b) wherein the deprotected hydroxyl of the coupled nucleoside in one cycle of the steps serves as the hydroxyl group of substrate bound moieties in the next cycle, so as to form the addressable array with different polynucleotide sequences at different addresses.

13. A method according to claim 12 wherein in step (a) the nucleosides to be coupled at respective addresses are deposited as droplets at those addresses.

14. A method according to claim 12 wherein in step (b) all of the substrate is simultaneously exposed to the composition.

15. A method according to claim 12 wherein the second nucleoside is a phosphoramidite.

16. A method according to claim 12 wherein the non-carbonate protecting group is an acid labile protecting group and the composition comprises an acid to remove the non-carbonate protecting group.

17. A method according to claim 16 wherein the composition comprises an acetic acid and iodine or an organic peroxide in a solvent which is primarily non-aqueous.

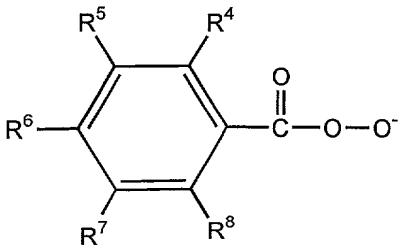
18. A method according to claim 17 wherein the composition comprises no more than 5% of the acetic acid and no more than 5% of iodine.

19. A method according to claim 17 wherein the composition comprises no more than 10% di- or tri-chloracetic acid and no more than 5% iodine.

20. A method according to claim 12 wherein the non-carbonate protecting group is labile under nucleophilic attack under neutral or mildly basic conditions and the composition comprises a nucleophile that exhibits an alpha effect at neutral to mildly basic pH.

21. The method of claim 20 wherein the nucleophile is an inorganic peroxide of the formula M+OOH-, wherein M+ is a counterion selected from the group consisting of H+, Li+, Na+, K+, Rb+ and Cs+.

22. The method of claim 20, wherein the nucleophile is an organic peroxide of the formula (V), (VI) or (VII),



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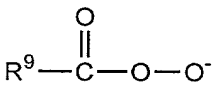

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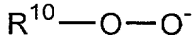

(VII)

in which R4 through R10 are hydrocarbyl optionally substituted with one or more nonhydrocarbyl substituents and optionally containing one or more nonhydrocarbyl linkages.

23. The method of claim 20 wherein the nucleophile is one of t-butyl hydroperoxide, m-chloroperoxybenzoic acid, or mixtures thereof.

24. A method according to claim 12 wherein the method is executed at each of at least 1000 addresses.

25. A method for making an oligonucleotide array made up of array features each presenting a specified oligonucleotide sequence at an address on an array substrate, the method comprising steps of:

providing a hydroxyl-derivatized array substrate and treating the array substrate to protect hydroxyl moieties on the derivatized surface from reaction with phosphoramidites,

then iteratively carrying out the steps of (i) applying droplets of an alpha effect nucleophile to effect deprotection of hydroxyl moieties at selected addresses, and (ii) flooding the array substrate with a medium containing a

selected monomeric nucleoside phosphoramidite having a carbonate-protected hydroxyl group, to permit covalent attachment of the selected nucleoside to the deprotected hydroxyl moieties at the selected addresses.